

Economic burden of hospitalizations for acute myeloid leukemia in remission in the United States:
A retrospective analysis of an administrative claims database

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Background

- Management of acute myeloid leukemia (AML) is associated with substantial economic burden^{1,2}
- In the continuum of AML care, the highest costs are related to relapsed/refractory disease, and hospitalization is the largest component of direct healthcare costs²
- Results from the phase 3 QUAZAR AML-001 trial showed that oral azacitidine as maintenance therapy was associated with significantly prolonged overall survival (OS) and relapse-free survival (RFS) vs placebo in patients with AML in first remission after intensive chemotherapy³
- Significantly improved duration of remission (DOR) with Oral-AZA may translate into substantial economic benefits associated with reduced rates of hospitalization and fewer days in hospital^{4,5}
- The real-world economic benefit of prolonging DOR for patients with AML remains insufficiently studied

Objective

- This study examined the economic burden of hospitalizations among patients with newly diagnosed AML in remission from a retrospective analysis of real-world data from a US claims database

Methods

- Using a retrospective cohort design, adult patients with an AML diagnosis (ICD-9-CM/ICD-10-CM) who achieved remission after first-line induction chemotherapy in the period from 1 July 2012 to 30 September 2019 were identified from the Optum® Clinformatics® Data Mart administrative claims health database
- Patients were required to have at least 6 months of continuous enrollment, with pharmacy benefits, prior to the index diagnosis date (baseline)
- Inclusion and exclusion criteria were applied to match the QUAZAR AML-001 trial population³ (**Table 1**).
- Patients were followed from the time of remission after induction therapy, with or without consolidation, to the end of the follow-up period
- Eligible patients were organized into cohorts based on the overall median DOR:
 - Cohort A had < median DOR
 - Cohort B had ≥ median DOR
- Patient demographics and disease characteristics at baseline are analyzed descriptively
- Hospitalization incidence and duration during the follow-up period were calculated using a standard cost per-patient-per-year (PPPY) metric. Generalized estimating equations (GEE) clustered on the patient were used to compare incidence and duration of hospitalizations between cohorts
- Hospitalization-related costs between cohorts were compared using a generalized linear model with gamma distribution and log-link function
- All costs were adjusted for inflation and reported in 2019 US dollars (USD)

Table 1. Selection of the study cohort

Step	Selection criteria	N	Change from prior step
1	≥ 1 inpatient or ≥ 2 outpatient claims with AML ^a within a period of 90 days between 01-Jul-2012 and 30-Sep-2019	12,155	—
2	Continuous enrollment for ≥ 180 days before the index diagnosis date	9,622	-20.8%
3	No prior diagnosis of any primary proliferative disorder or malignancy (excl. myelofibrosis, myelodysplastic syndromes, myeloproliferative disorders/neoplasms, non-melanoma skin cancers), or AML in remission, ^b in the 180 days before the index diagnosis date	4,478	-53.5%
4	Did not receive first-line systemic induction therapy for AML in the 180 days before the index diagnosis date	3,922	-12.4%
5	Received first-line systemic induction therapy for AML on or after the index diagnosis date	2,164	-44.8%
5a	The index remission date was after start and within 180 days of first-line treatment	823	-62.0%
5b	The remission index date was before the start of second-line treatment	802	-2.6%
6	The end of follow-up was on or after the index remission date	799	-0.4%
7	Age was ≥ 18 years at the index diagnosis date	750	-6.1%
8	No bone marrow or stem cell transplantation at any time	508	-32.3%
9	No diagnosis of AML-M3 (APL ^c), or treatment with arsenic trioxide or all-trans retinoic acid	451	-11.2%
10	No capitated enrollment month(s) from the index remission date to the end of follow-up	451	NA

^aICD-9-CM diagnosis codes 205.00; ICD-10-CM diagnosis codes C92.00, C92.60, C92.A0.
^bICD-9-CM diagnosis codes 205.01; ICD-10-CM diagnosis codes C92.01, C92.61, C92.A1.
^cICD-10-CM diagnosis code APL C92.4x.
AML, acute myeloid leukemia; APL, acute promyelocytic leukemia; ICD, International Classification of Disease; NA, not applicable.

Results

Patient characteristics

- Overall, a total of 451 patients were selected for the analysis (**Table 1**)
- Median DOR was 125 days
 - Cohort A included 220 patients with < median DOR
 - Cohort B included 231 patients with ≥ median DOR
- Both cohorts were comparable regarding age, comorbidity index and geographic region, though a greater proportion of patients were female in Cohort B (40.5% in Cohort A vs 52.4% in Cohort B; *P* = 0.0111) (**Table 2**)
- There was no statistically significant difference in median time from diagnosis between Cohort A and Cohort B (53.5 vs 55.0 days, respectively; *P* = 0.7145), nor from induction to first remission (48.0 vs 48.0 days, *P* = 0.6136) (**Table 2**)
- The median time from first remission to relapse or end of follow-up was shorter for Cohort A than for Cohort B (49 vs 300 days; *P* < 0.0001) (**Table 3**)

Table 1. Patient characteristics

	All Patients N = 451	Cohort A n = 220	Cohort B (≥ Median DOR) n = 231	P value, Cohort A vs. Cohort B
Sex, n (%)				
Male	241 (53.4)	131 (59.5)	110 (47.6)	0.0111
Female	210 (46.6)	89 (40.5)	121 (52.4)	
Age at AML diagnosis, years				
Mean [SD]	62.8 [14.7]	64.0 [14.2]	61.7 [15.2]	0.0991
Median (IQR)	66.0 (55.0, 73.0)	67.0 (57.0, 73.0)	65.0 (54.0, 72.0)	0.0812
Age subgroup at diagnosis, n (%)				
< 55 years	107 (23.7)	46 (20.9)	61 (26.4)	0.2402
55 to 64 years	91 (20.2)	42 (19.1)	49 (21.2)	
65 to 74 years	166 (36.8)	91 (41.4)	75 (32.5)	
≥ 75 years	87 (19.3)	41 (18.6)	46 (19.9)	
Geographic region, n (%)				
Northeast	64 (14.2)	30 (13.6)	34 (14.7)	0.6148 ^a
North-central	114 (25.3)	59 (26.8)	55 (23.8)	
South	183 (40.6)	92 (41.8)	91 (39.4)	
West	86 (19.1)	37 (16.8)	49 (21.2)	
Missing/unknown	4 (0.9)	2 (0.9)	2 (0.9)	
Charlson comorbidity index at diagnosis, n (%)				
Mean [SD]	1.7 [1.6]	1.7 [1.6]	1.6 [1.5]	0.7723
Median (IQR)	2.0 (0.0, 3.0)	2.0 (0.0, 3.0)	2.0 (0.0, 3.0)	0.9082
Insurance plan type at diagnosis, n (%)				
Commercial	204 (45.2)	90 (40.9)	114 (49.4)	0.0718
Medicare	247 (54.8)	130 (59.1)	117 (50.6)	
Time from diagnosis to first remission, days				
Mean [SD]	70.2 [67.7]	71.2 [82.5]	69.3 [49.9]	0.7644
Median (IQR)	54.0 (39.0, 87.0)	53.5 (37.5, 85.5)	55.0 (39.0, 88.0)	0.7145
Time from induction to first remission, days				
Mean [SD]	56.9 [36.3]	56.3 [37.4]	57.5 [35.3]	0.7326
Median (IQR)	48.0 (33.0, 76.0)	48.0 (32.5, 73.0)	48.0 (33.0, 77.0)	0.6136

^aPatients with a missing or unknown variable were excluded from the statistical test.
AML, acute myeloid leukemia; DOR, duration of remission; IQR, interquartile range; SD, standard deviation.

Cost analysis

- The mean PPPY total number of hospitalizations was higher in Cohort A than in Cohort B (4.71 vs 2.68, respectively), as was the mean PPPY total length of hospital stays (43.88 vs 23.59 days) (**Table 3**)
- Estimated mean PPPY total hospitalization-related costs were \$242,511 in Cohort A, compared with \$132,554 in Cohort B
- The Cumulative mean hospitalization cost per patient was \$61,372 higher in Cohort A at 12 months and \$108,593 higher at 24 months (**Figure 1**)
- Sensitivity analyses show that these results are relatively constant regarding a range variation of follow-up period (**Table 4**)
- Multivariate GEE and GLM models with adjustment for baseline covariates, including age, sex, comorbidity index, geographic region, and insurance type, identified that prolonged DOR was significantly associated with reduced number, length, and cost of hospitalization (*P* < 0.001, all comparisons) (**Table 5**)

Table 3. Hospitalization incidences, durations, and costs from time of remission to end of follow-up

	All Patients N = 451	Cohort A n = 220	Cohort B (≥ Median DOR) n = 231
Total number of hospitalizations	1346	503	843
Median time from remission to relapse/end of follow-up, days	125.0	49.0	300.0
Number of hospitalizations PPPY	3.19	4.71	2.68
Total duration of hospital stay, days	12,123	4,688	7,435
Duration of hospital stay PPPY, days	28.73	43.88	23.59
Length of stay per hospitalization, days	9.0	9.3	8.8
Cost of hospitalization PPPY, USD ^a	\$160,395	\$242,511	\$132,554
Cost of hospitalization per stay, USD ^a	\$50,283	\$51,512	\$49,549
Cost of hospitalization per day of stay, USD ^a	\$5,583	\$5,527	\$5,618

^aCosts adjusted for inflation to 2019 USD.
DOR, duration of remission; PPPY, per patient per year; USD, United States dollar.

Figure 1. Cumulative per-patient hospitalization costs over time

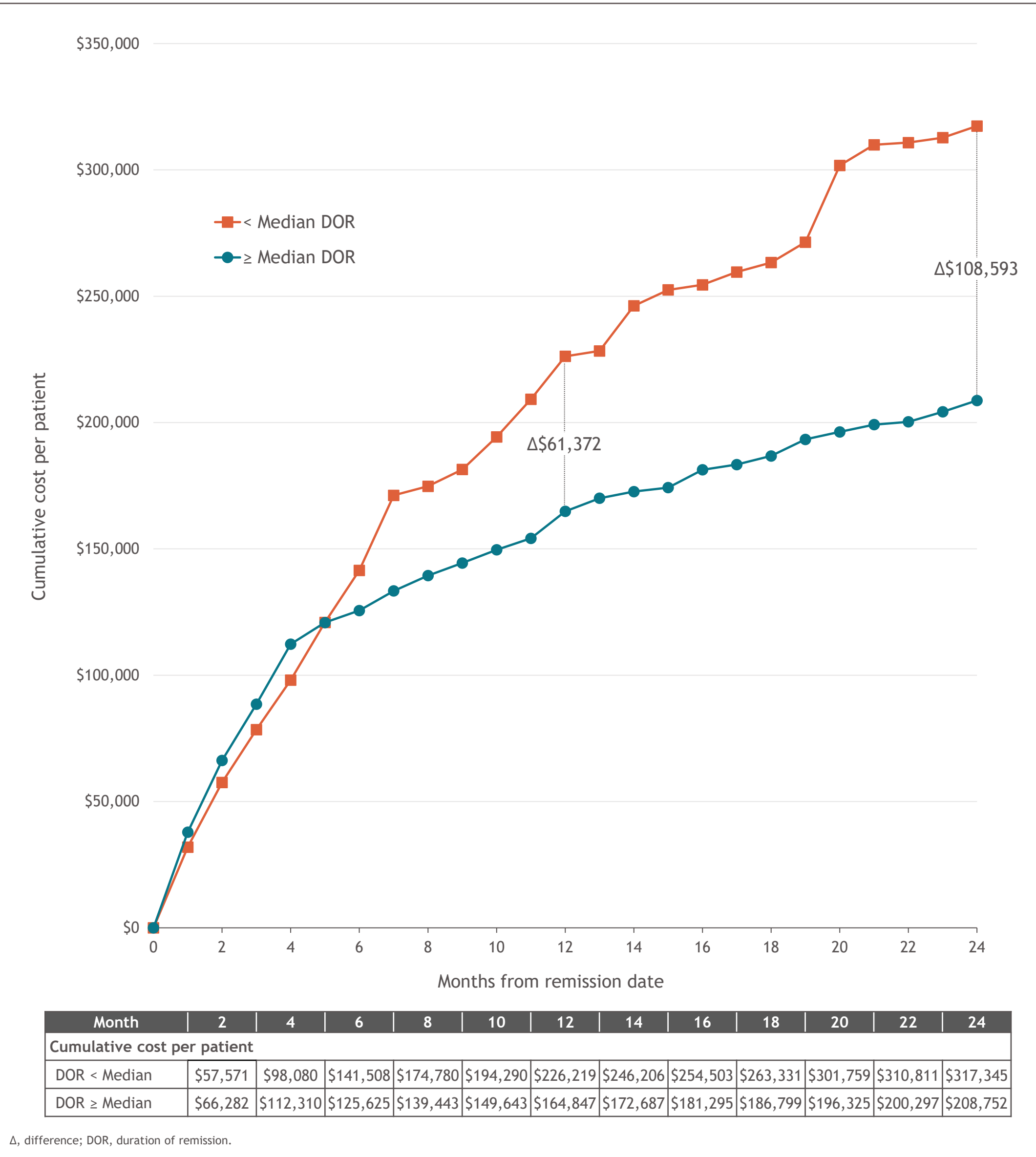


Table 4. Aggregate incidence of hospitalization, days, and costs over different follow-up periods.

Mo of FU post-remission	Statistics	All Patients (N = 451)	Cohort A n = 220	Cohort B (≥ Median DOR) n = 231
≥ 6 mo	Total number of pts, n	226	52	174
	Mean number of hospitalizations, n	2.98	3.23	2.91
	Mean length of hospital stay, days	24.68	28.69	23.48
	Mean cost of hospitalization, USD	\$142,650	\$164,642	\$136,078
≥ 12 mo	Total number of pts, n	133	24	109
	Mean number of hospitalizations, n	3.47	3.42	3.48
	Mean length of hospital stay, days	27.59	30.33	26.99
	Mean cost of hospitalization, USD	\$159,856	\$185,750	\$154,154
≥ 18 mo	Total number of pts, n	76	17	59
	Mean number of hospitalizations, n	3.88	4.12	3.81
	Mean length of hospital stay, days	31.54	38.29	29.59
	Mean cost of hospitalization, USD	\$173,130	\$222,006	\$159,047

DOR, duration of remission; FU, follow-up; mo, months; USD, United States dollar.

Table 5. Adjusted analyses of hospitalization incidence, duration, and cost from remission to end of follow-up

Variable	Cohort A n = 220	Cohort B (≥ Median DOR) n = 231	Difference, Cohort B vs. Cohort A	P value
Cost of hospitalization PPPY, USD [95% CI]	\$235,722 [\$191,794 to \$279,650]	\$134,959 [\$112,896 to \$157,022]	-\$100,763 [-\$150,325 to -\$51,201]	< 0.001
Duration of hospital stay PPPY, days [95% CI]	44.00 [40.43, 47.57]	27.16 [25.52, 28.80]	-16.84 [-20.79, -12.90]	< 0.001
Number of hospitalizations PPPY [95% CI]	5.11 [4.37, 5.85]	3.00 [2.61, 3.39]	-2.11 [-2.95, -1.28]	< 0.001
Probability of ≥ 1 hospitalization, % [95% CI]	78.62 [72.66, 84.58]	90.64 [86.89, 94.40]	12.03 [5.25, 18.80]	0.001

PPPY=Total cost/total years of follow-up.
CI, confidence interval; DOR, duration of remission; PPPY, per patient per year; USD, United States dollar.

Limitations

- As this study is limited to patients with Commercial or Medicare coverage, the results may not be generalizable to AML patients with other types of insurance
- This analysis only included patients with ≥ 6 months of continuous enrollment before their indexed remission date; therefore, patients who had intermittent healthcare coverage were not included
- As with any claims database analysis, misclassification of patients and underestimation of comorbidities may occur due to coding limitations and potential data entry errors
- Despite these limitations, retrospective database studies allow observation of patients who are often underrepresented in clinical trials, such as older patients and those with comorbidities

Conclusions

- In a real-world setting, prolonged remission was associated with significantly lower rates and durations of hospitalization in patients with AML in remission following induction chemotherapy, which were estimated to result in substantial cumulative cost savings
- These data underscore the unmet need for effective therapies aimed at maintaining remission in patients with AML
- In an era of increasing scrutiny of the cost-effectiveness of prolonged treatment, it is important to weigh treatment costs against the potential economic benefit of reducing healthcare resource utilization

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